Study of Pharmacogenomics Information Seeking

CPIC

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Outline

- **Introduction**
  - Information Need/Genomics
  - Adverse Drug Events/Pharmacogenomics Information Gap
- **Methodology**
  - Cognitive model of information retrieval: *Berry Picking*
- **Results**
- **Conclusion**

How much can be processed in one moment?

1) Patient

2) Disease

3) Drug

4) Gene

5) Information Chunk A

6) Information Chunk B

7) My schedule

Miller, G. A. (1956). "The magical number seven, plus or minus two: Some limits on our capacity for processing information". Psychological Review 63 (2): 81–97.

If no one searches for the information does it exist?

Many clinicians appear to assume a high cost/low benefit for pharmacogenomics testing.

"(e)fficacy beliefs in part determine outcome expectations" and that "(m)ost people engage in tasks in which they feel competent and confident and avoid those in which they do not" – A. Bandura, Theory of Self Efficacy

'inertia of current practice', 'lack of self-efficacy' - Cabana et al, Why don't physicians follow clinical practice guidelines

Bandura A. Self-Efficacy. In: Ramachaudran VS, editor. Encyclopedia of human behavior. New York: Academic Press; 1994. p. 77–81.

Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines?: A framework for improvement. JAMA. 1999 Oct 20;282(15):1458–65.

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General Need for information

0.57 questions per patient go answered in course of clinical care*

On average up to 2 min is spent seeking information*

- "How does genetic variation effect the course of treatment?"
- "Is there a genetic test to determine risk?"
- "Is there a genetic test to confirm suspicion of genetic interaction?"

*Del Fiol, G., Workman, T. E. & Gorman, P. N. Clinical questions raised by clinicians at the point of care: a systematic review. JAMA Intern. Med. 174, 710–718 (2014).

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Adverse Drug Events

!

100,000 

2,000,000 

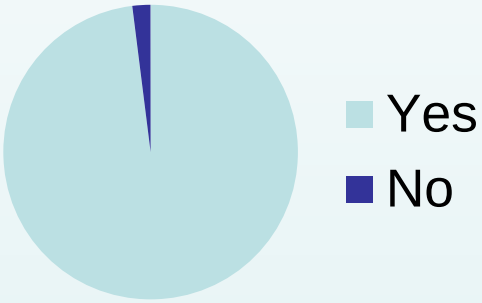
136,000,000,000 $

Adams, J. (2008) Pharmacogenomics and personalized medicine. Nature Education 1(1):194

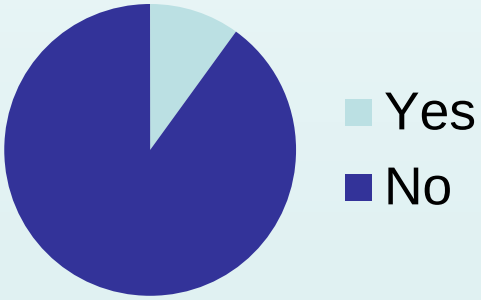
Pharmacogenomics Need for Information

What Physicians said

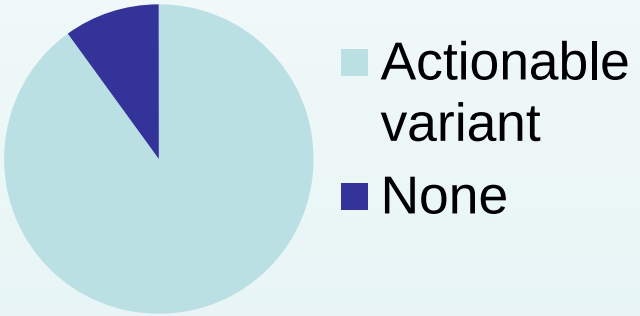
Beneficial to patients?



Sufficient knowledge?



The data speaks



Do patients with WGS have 1 of 5 pharmacogenomically actionable genetic alleles?

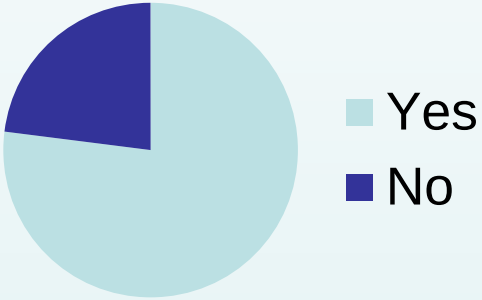
Stanek et al. Adoption of Pharmacogenomic Testing by US Physicians: Results of a Nationwide Survey. Clin Pharmacol Ther. 2012 Mar;91(3):450–8.

Van Driest et al. Clinically Actionable Genotypes Among 10,000 Patients With Preemptive Pharmacogenomic Testing. Clin Pharmacol Ther [Internet]. 2014 Jan 22 [

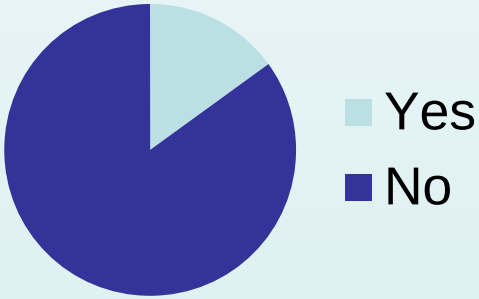
Recent supporting data

What Physicians said

Confident in understanding of Basic Genetics?



Confident in understanding when and how to incorporate genomic medicine?



Pennington et al. Genomic decision support needs in pediatric primary care JAMIA, 2017 July, 24(4): 851–856.

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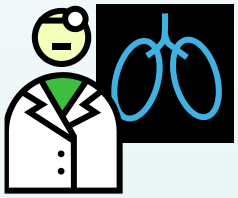
PHYSICIANS' PHARMACOGENOMICS INFORMATION SEEKING BEHAVIOR AND NEEDS : A STUDY WITH CASE VIGNETTES

Methods: Brief

Mixed-method approach



Case vignettes
developed with experts

Six Subjects

Pre-survey

Screen/Audio capture

Post-survey

Deepening Interview

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Methods: summary case vignettes

Case Vignette	Disease or Condition	Medication focus	Problem	Patient	Main information seeking driver
1	Guacher's disease	Enzyme Replacement Therapy	Hereditary risk	Prospective child of at risk parents	Parents desire to be prepared
2	Asthma	Albuterol	Worsening symptoms while on treatment	Pediatric male, no apparent environmental factors, twin sister with same problem	Father's concern
3	Percutaneous coronary intervention	Clopidogrel	Loading dose prescription	65 –year old male, past smoker, no history of bleeding or increased clotting	Patient's concern

Case study 3

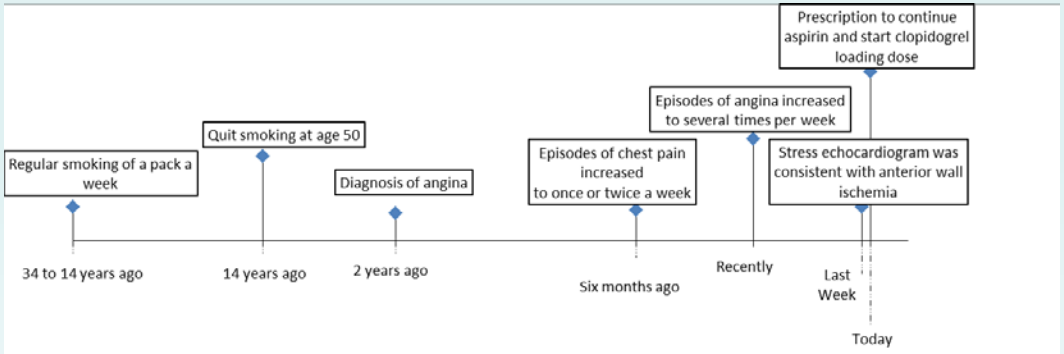
Frank is a 64-year old male with coronary artery disease, who you are meeting in your office prior to planned coronary angiography/stenting (PCI) for angina symptoms. Having quit smoking at age 50, after 20 years at a pack a week, he seemed to be in excellent health. However, about two years ago he was diagnoses with angina and given a prescription for aspirin (75mg/day), simvastatin (40 mg/day), and a recommendation for lifestyle change. At that time he started an exercise regimen and reduced fat intake in his diet. Despite these lifestyle changes, six months ago he noted that episodes of chest pain increased to about once or twice per week precipitated by exercise or stress and relieved by rest. But recently the angina episodes have increased to several times per week. Last week a stress echocardiogram demonstrated anterior wall ischemia and angiography with possible PCI was recommended.

As per ACC guidelines, aspirin (75mg/day) will be continued and Frank has been prescribed clopidogrel (300 mg loading dose, followed by 75 mg/day). Reviewing his medical history there is no evidence of an increased risk of bleeding, nor is there a family history of increased clotting. During the consultation prior to the procedure, Frank mentions that his friend Sam was given a high dose of clopidogrel because Sam was determined to be resistant, due to a variation in CYP2C19 gene function. Frank asks you if he should also be tested for the genetic variant.

Frank's question reminds you that in the morning of the consultation one of your colleagues was telling you about how variations in CYP2C19 can alter the metabolism of clopidogrel such that less active drug is present. You also recall reading about clopidogrel and pharmacogenomics testing, but you cannot quite remember all the details.

Please search UpToDate, the CPIC clopidogrel summary from PharmGKB, and the clopidogrel CPIC guideline till you feel confidant to manage the case and address Frank's question on pharmacogenomics testing.

post-Case
Time Line



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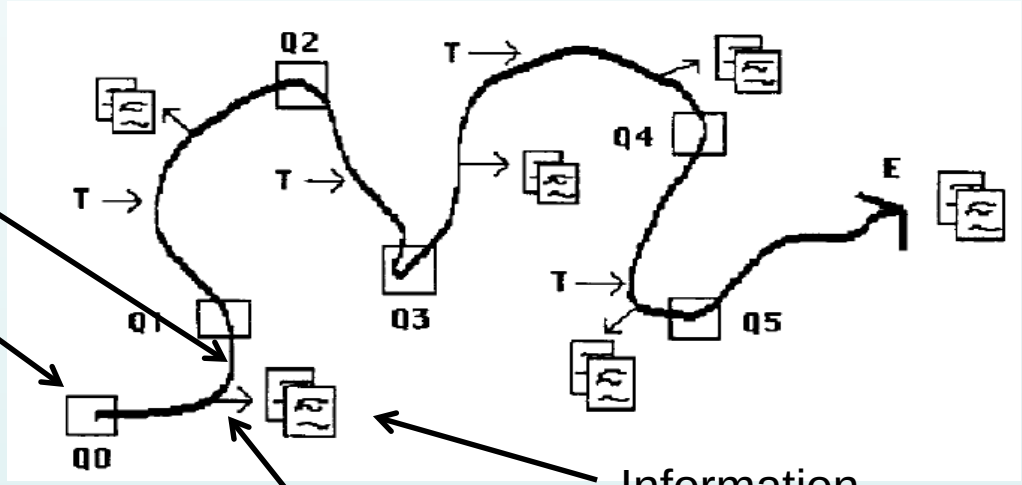
Methods: Qualitative Data analysis

Coded Needs using Berry-picking as a framework

Cognitive model of information retrieval



Independent coding followed by reconciliation, and Theme analysis

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Information needs categories and themes

Category	Theme
Is there an alternative therapy that obviates the need for genetic testing?	Alternative therapy options
Clear, reliable guidance on genetic testing: when and how	Specific, actionable, clinical guidance from authoritative sources Guidance on optimal approach to genetic testing Logistics of testing
How often might genetic testing be indicated?	Prevalence of genetic variation Indications for genetic testing
How important is genetic testing to care of my patient and what is the evidence?	Clinical impact of genetic testing Practice changing evidence
Help in understanding genetic effects	Role of genetics in the manifestation of the disease Understanding general molecular effect of genetic variant
Aid in searching for information	Help with search terms

Themes

Alternative therapy options

"just switch to something else."

Specific, actionable, clinical guidance from authoritative sources

"going for a bottom-line", "with the authorities, with the experts, with the review of the literature, American Heart Association and the rest"

Themes

Guidance on optimal approach to genetic testing

"indication that I should select a particular genetic test option"

Logistics of testing

"if a test even exists and how much it costs", "can they turn [the genetic test] around?", presence of experts

Themes

Prevalence of genetic variation

“just how many individuals do I need to test before I find”

Indications for genetic testing

"a bulleted list that says risk factors for testing."

Themes

Clinical Impact of genetic testing

"…so, they're suggesting another drug for intermediate metabolizers."

"I like this failure thing because I wonder if [genetics] might have something to do with [severity of] failure".

Themes

Practice-changing evidence

"But essentially you know whenever [the] clinical literature says 'data suggests' or 'maybe relevant,' that sort of thing, you realize that the evidence basis is still in its nascence. It may still be weak. "

Themes

Role of genetics in the manifestation of the disease

"*I would want to know about the genetic variant effects that are associated with worsening asthma symptoms*"

Understanding general molecular effect of genetic variant

"trying to recall my molecular biology"

Themes

Help with search terms

“98 times out of 100, I get a couple of search terms that I can screen down, I can find out exactly what I want to go to very quickly.”

Information Seeking Behavior

- 8 min searching
- Frequently only one search query used
- On average 8 navigation events per subject per case
- Majority of time, 30 seconds before navigating away from content

Limitations

- Formative study
- 6 subjects
- No time constraint
- Primarily UpToDate

Take Home Message

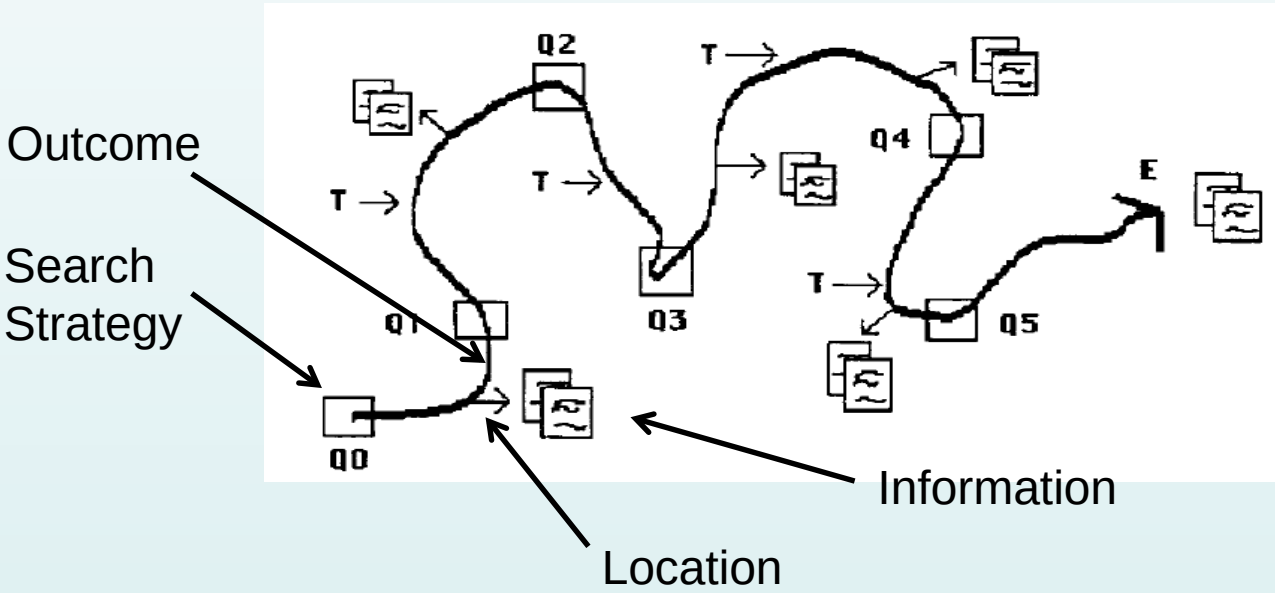
- 8 min of search time >>> 2 min average time clinicians search for information
- Information Topics: Viability of Alternative Therapy, Logistics, Evidence, Brief-Authoritative Recommendations, Access to Experts
- Snippets of information consumable in 30 seconds would be best
- Access to data which drove search
- Help with search terms

Summary of Design Implications

Recommendation	Guidance
Facilitate berry-picking strategy	Provide multiple information berries in single content view. E.g. a bulleted synopsis of alternative treatments, evidence (including demographic data), indications, cost, other testing logistics
Facilitate berry-picking strategy	Guide user through information gathering process. E.g. provide basic pharmacogenomics information, such as the strength of clinical evidence, prior to providing logistical details
Provide clarity of sought after details	Unmask details which are hard to find and sought after. E.g. Clarify demographic prevalence data, and provide clear indications of alternative therapy that obviates the need for pharmacogenomic testing
Provide information on logistics	List laboratories offering test(s), provide test availability, highlight time to result, indicate insurance coverage and cost of test(s), provide a means to access an expert (either colleague who frequently uses the test or a pharmacogenomics expert)
Provide navigation support	Meaningful content headings and hyperlink labels.
Reduce navigation effort and short-term memory overload	Provide context specific information juxtaposed to relevant patient data

Something to Consider

UI that records and adapts to users' search process – e.g. a search wizard that asks specific questions.



H: Matching the process of Berry-picking (i.e. providing ordered information snippets) will enhance understanding.

Acknowledgements

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ClinGen EMR WG

Research Subjects (i.e. Informants)

You - CPIC

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Some advances

- PharmGKB has a new(er) API which can be used to meet some of the needs noted
- Genetic Testing Registry provides some Logistics data (https://www.ncbi.nlm.nih.gov/gtr/tests/500489/howtoorder/)